REMARKS

Claims 1-16 and 19-21 were pending prior to the present Amendment, and new claims 22-25 have been added herein. Claims 1-16 and 19-25 are now therefore currently pending in the present application.

The Applicants gratefully acknowledge the Examiner's finding that claims 7, 8, 19, and 20 are allowable over the prior art of record, and are currently only objected to in view of being dependent on a rejected claim. The Applicants respectfully request reconsideration of this objection in view of the Applicants' comments below.

Claims 1, 4, and 6 have been amended in order to correct minor informalities noted in the Office Action dated May 20, 2009. No new matter has been added to this application by the amendments made herein, with support being found in the specification, claims and figures as filed. Support for new claim 24, for example, can be found on page 3, lines 7-9 of the present application, which states that "Preferred alkyl groups contain 1 to 10 carbon atoms. Suitable alkyl groups include methyl, ethyl, and the like..." In view of the foregoing, the Applicants respectfully request entry of this Amendment and consideration of the present application as amended herein.

Objections to the Claims

Claims 1-9 and 19-20 were objected to in view of certain informalities noted in the Office Action dated May 20, 2009. The Applicants have amended claims 1 and 4 in order to correct these informalities. The Applicants therefore respectfully request that the objections to claims 1-9 and 19-20 be withdrawn.

Rejections under 35 U.S.C. §112, Second Paragraph

Claim 6 was rejected under 35 U.S.C. §112, second paragraph as being indefinite. The Applicants have amended claim 6 in order to clarify this claim. In view of this, the Applicants respectfully request that the rejection of claim 6 under 35 U.S.C. §112, second paragraph be withdrawn.

Provisional Non-Statutory Double Patenting

Claims 1-5 and 9 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting in view of claims 1-5 and 9 of Application No. 10/986,485. Application No. 10/986,485 has now gone abandoned, making this ground of rejection moot. In view of this, the Applicants respectfully request that the rejection of claims 1-5 and 9 on the ground of nonstatutory obviousness-type double patenting be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-6 and 9 were rejected under 35 U.S.C. § 103(a) as being unpatentable over International Patent Publication No. WO 03/011396 to Fick. The Fick reference teaches tetrahydroindolone arylpiperazine compounds useful in treating anti-psychotic disorders. As noted on page 9 of the Office Action, "Fick et al. do not specifically teach compounds wherein R6 is an alkyl group." The Examiner's position, though, is that the substitution of a methyl group for a hydrogen group, such as at the R6 position of the present compounds, is not patentable absent unexpected or unobvious results.

The Applicants respectfully submit, however, that the addition of a methyl group to a compound having neurological properties, such as the compounds of the present invention, is not an obvious substitution in view of prior art research showing that the effect of such a substitution is unpredictable and may in fact be deleterious. In support of this position, the Applicants are submitting herewith as Attachment 1 an article by Tecle, et al. [Tecle, H. et al., "CI-1017, a functionally M_1-selective muscarinic agonist: design, synthesis, and preclinical pharmacology," Pharmaceutica Acta Helvetiae, 74:141-148 (2000)]. The Tecle article reports the results of tests performed on compounds having activity at the muscarinic receptor, which is present on neurons throughout the central nervous system and is involved in mediating emotional and cognitive functions, among other things.

The Tecle reference reports in particular that the binding affinity of the muscarinic receptor agonist arecoline is significantly inhibited by the addition of a single methyl group to the ring moiety of this compound. Arecoline is a naturally occurring alkaloid which has been shown to ameliorate the symptoms of cognitive disorders in patients diagnosed with presenile primary degenerative dementia or Alzheimer's Disease. As shown in Table 3 on page 143 of the

Tecle reference, when a single methyl group was added to positions R2, R4, or R5 of the ring moiety of arecoline (i.e., in compounds 1b – 1d), the IC_{50} of the compound increased by between 10-fold and more than 100-fold compared to arecoline (compound 1a). The IC_{50}, or half maximal inhibitory concentration, is a measure of the effectiveness of a compound in inhibiting biological or biochemical function, and an increase in this concentration means that more of the compound is required to achieve the same efficacy, in this case between ten and more than one hundred times more. The Tecle reference summarized this result by stating on page 145 that "steric bulk in the ring ... moiety drastically reduced binding affinity and efficacy at the muscarinic receptor" (left hand column, section 3.1).

It is therefore unexpected that the present compounds not only retain effectiveness as neurological agents despite the substitution of methyl and other chemical groups at the R6 position, but as described in the previously submitted Declaration of David Helton, the present compounds in fact exhibit improved properties compared to the prior art Fick compounds. The Applicants therefore respectfully submit that the addition of a methyl group at the R6 position of the present compounds is not an obvious substitution, and that the pending claims are patentable over the Fick reference. In view of this, the Applicants further respectfully request that the rejection of claims 1-6 and 9 under 35 U.S.C. § 103(a) as being unpatentable over International Patent Publication No. WO 03/011396 to Fick be withdrawn.

Restriction Requirement

The Office Action dated May 20, 2009 affirms the Examiner's prior finding of a lack of unity between the invention of claims 1-9, 19 and 20 (Group I) and the invention of claims 10-16 and 21 (Group II). This assertion is based on the position that prior art compounds (i.e., those of PCT Publication No. WO 03/011396 to Fick) having a hydrogen at the R6 position of the compound of claim 1 render obvious the present compounds having a methyl group at this position. In view of Applicants' comments above regarding the nonobviousness of claim 1 over the Fick reference, the Applicants respectfully submit that the prior art Fick compounds do not render the presently claimed compounds obvious. The Applicants therefore respectfully request reconsideration and withdrawal of the restriction requirement in the present application.

Conclusion

The Applicant believes that all pending claims are in condition for allowance, and a Notice of Allowance is thus respectfully requested. If, however, there remain any issues which can be addressed by telephone, the Examiner is encouraged to contact the undersigned at the telephone number listed below.

Please charge any fees due in connection with this Amendment or credit any overpayment to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON MAK ROSE & ANDERSON

Date: October 20, 2009

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